

Page 10, replace the paragraph starting line 26 and ending in page 11, line 2, with:

Sub B2
A2
The dormancy-control substance according to the present invention has an amino acid sequence: Asp-Ile-Leu-Arg-Gly (SEQ ID NO:1), has a C-terminal amide group and has a molecular weight of 570.959.

Page 12, replace the paragraph starting line 4 with:

Sub B3
A3
In addition, the living cell-control agent according to the present invention, for instance, a cancer cell growth-inhibitory agent comprises, as an effective component, a peptide, which has an amino acid sequence: Asp-Ile-Leu-Arg-Gly (SEQ ID NO:1), which has a C-terminal amide group and which has a molecular weight of 570.959. This peptide is one derived from the pre-larvae of *Antheraea yamamai* as already discussed above and can be prepared by the same method used above.

Page 12, replace the paragraph starting line 11 with:

Sub B4
A4
Furthermore, the living cell-control agent according to the present invention, for instance, a cancer cell growth-inhibitory agent may be one comprising, as an effective component, a peptide having an amino acid sequence: Ile-Leu-Arg-Gly (SEQ ID NO:2), which corresponds to that specified as SEQ ID NO:1 from which the N-terminal Asp residue is deleted, which has a C-terminal amide group and which has a molecular weight of 456.58.

Page 15, replace line 16 with:

AS weight of a synthetic peptide (Asp-Ile-Leu-Arg-Gly-NH₂, SEQ ID NO:1 having the C-terminal amidated) having an amino acid sequence and C-terminal identical

Page 15, replace line 20 with:

AB weight of a synthetic peptide (Asp-Ile-Leu-Arg-Gly-OH, SEQ ID NO:1) having an amino acid sequence identical to that of the

Page 16, replace the paragraph starting line 1 with:

Fig. 9 is a micrograph showing the morphological change and growth inhibition observed for rat hepatoma cells (dRLh84) when using DILRG-NH₂ (the peptide of SEQ ID NO:1 having the C-terminal amidated) or DILRG-COOH (SEQ ID NO:1).

Page 16, replace the paragraph starting line 4 with:

Fig. 10 is a graph showing the growth-control effect of DILRG-NH₂ (the peptide of SEQ ID NO:1 having the C-terminal amidated) or DILRG-COOH (SEQ ID NO:1) on the rat hepatoma cells (dRLh84) in terms of the relation between the concentration and the viable cell count.

Page 16, replace the paragraph starting line 7 with:

Fig. 11 is a graph showing the growth-control effect of DILRG-NH₂ (the peptide of SEQ ID NO:1 having the C-terminal amidated) or PBS(-) on the rat hepatoma cells (dRLh84) in terms of the relation between the cultivation time and the viable cell count.

Page 16, replace the paragraph starting line 14 with:

Fig. 13 is a graph showing the growth-control effect of DILRG-NH₂ (the peptide of SEQ ID NO:1 having the C-terminal amidated) on the rat hepatoma cells (dRLh84), while comparing it with those observed for other substances.

Page 17, replace the paragraph starting line 6 with:

As has been discussed above, the dormancy-control substance according to the present invention is a novel peptide having a dormancy-control function, 5 amino acid residues thereof from the N-terminal are Asp-Ile-Leu-Arg-Gly (SEQ ID NO:1), and it is a low molecular weight substance (molecular weight: 570.959) and does not have a free oxidized C-terminal, but has a C-terminal carrying an amide group. This is clear from the fact that only the peptide whose C-terminal carries an amide group possesses such a control function as demonstrated by the biological assay concerning the compounds prepared in Examples as will be described below. This substance can be isolated and purified from, for instance, the pre-larvae of *Antheraea yamamai* or alternatively, it can be synthesized according to the conventional methods since the amino acid sequence thereof is elucidated.

Page 18, replace the paragraph starting line 3 with:

As has been discussed above, the amino acid sequence of the repressive factor of the peptide, which is involved in the maintenance of the dormancy of the pre-larvae of *Antheraea yamamai*, is Asp-Ile-Leu-Arg-Gly-NH₂ (the peptide of SEQ ID NO:1 having

the C-terminal amidated). There has not any known peptide of this type of penta-peptide even when the computer research (BLAST and FASTA) is performed and thus the penta-peptide is a novel peptide having dormancy-control activity in the biological world. This is named *Antheraea yamamai*-Repressive Factor (abbreviation: Any-RF). Nobody has ever discovered the peptide comprising 5 amino acid residues and whose C-terminal carries an amide group in the free state in the biological world till the present invention has been completed. However, the amino acid segments identical to the foregoing one: ---Asp-Ile-Leu-Arg-Gly --- can be found in the amino acid sequence of several biological proteins. For instance, the amino acid sequence is identical to that found in the putative 22.1 KD protein (193 amino acid residues) of yeast (i.e. the fragment starting from 166th to 170th amino acid residues) and that found in the precursor (202 amino acid residues) of the human leukemia-inhibitory factor (i.e. the fragment extending from 142nd to 146th amino acid residues), according to the computer research. However, the functions of the amino acid sequences of these portions have not yet been elucidated at all. In other words, the amino acid sequence in the peptide of the present invention is sandwiched between - and C-terminals, the C-terminal has an amide group and the sequence is thus present in the free state, although the amino acid sequence of the present invention is identical to the fragment present in large protein sequences. Thus, there has never been discovered such an amino acid sequence present in the free state and possessing such a physiological function.

Page 36, replace the paragraph starting line 8 with:

Sub B13
1 A peptide whose primary structure was completely identical to that of the peptide isolated and purified by the foregoing procedures according to the present invention was prepared by the following method. More specifically, peptides Asp-Ile-Leu-Arg-Gly-NH₂ (the peptide of SEQ ID NO:1 having the C-terminal amidated) (abbreviated as DILRG-NH₂ or RF-NH₂) and Asp-Ile-Leu-Arg-Gly-COOH (SEQ ID NO:1) (abbreviated as DILRG-COOH or RF-COOH) were prepared according to the usual procedures using a peptide synthesizer (PSSM-8 available from Shimadzu Corporation). The purification of these peptides were carried out using a reverse phase column ULTRON VX-ODS (20mm x 250mm, available from Shinwa Kako K.K.) connected to an HPLC system (LC-10A, available from Shimadzu Corporation). The elution was carried out at a flow rate of 8 ml/min and using an acetonitrile concentration gradient (1 to 5% for 0 to 5 minutes; 5 to 60% for 5 to 35 minutes) in the presence of a 0.1% TFA to thus give active fractions. The absorbance at 220 nm was monitored. The purified peptide was mixed with an equivalent amount of a matrix (50% acetonitril/0.1% TFA saturated with α -CHCA) on the sample plate, followed by drying and confirmation of the purity thereof using MALDI-TOF MS (available from Voyager PerSeptive Biosystems Company).

Page 36, replace the paragraph starting line 24 and ending page 37, line 1 with:

Two kinds of peptides DILRG-NH₂ (the peptide of SEQ ID NO:1 having the C-terminal amidated) (purity: not less than 95%, determined using HPLC and TOF-MS) and DILRG-COOH (SEQ ID NO:1) (purity: not less than 95%, determined using HPLC

and TOF-MS) were synthesized according to the foregoing method and they were used
A14
in the following Examples.

Page 39, replace lines 16-18 with:

A15
purified product (Fig. 5), a maximum peak at 571.959 for the synthetic peptide: Asp-Ile-Leu-Arg-Gly-NH₂ (the peptide of SEQ ID NO:1 having the C-terminal amidated) (Fig. 6) and a maximum peak at 573.045 for the synthetic peptide: Asp-Ile-Leu-Arg-Gly-COOH (SEQ ID NO:1) (Fig. 7).

Page 42, replace the paragraph starting line 5 with:

S14
D12
A14
Consequently, the amino acid sequence of the repressive factor derived from *Antheraea yamamai* is Asp-Ile-Leu-Arg-Gly-NH₂ (the peptide of SEQ ID NO:1 having the C-terminal amidated) and the molecular weight thereof can be determined by subtracting 1 (mass of a proton) from the measured value of the mass spectrometric peak or 570.959.

Page 44, replace line 20 with:

A13
A peptide: Cys-ε-Acp-Asp-Ile-Leu-Arg-Gly-NH₂ (SEQ ID NO:3) (CXDILRG-NH₂) was

Page 47, replace the paragraph starting line 17 with:

A13
Rat hepatoma cells (dRLh84, 3 x 10⁵ cells) were cultured in a culture medium, to which the peptide (DILRG-NH₂, the peptide of SEQ ID NO:1 having the C-terminal amidated or DILRG-COOH, SEQ ID NO:1) was added in a predetermined amount (0,

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50, 100, 150, 200 $\mu\text{g/ml}$) in the presence of 5% CO_2 at 37°C for 40 hours. Thereafter, the culture medium was treated with trypan blue to determine the viable cell count. The results thus obtained are shown in Fig. 10.

Page 52, replace line 3 with:

1469
supplemented with PBS(-) and FMRF-NH₂ (SEQ ID NO:4), which is widely distributed from

Page 52, replace line 13, with:

the culture medium contained PBS(-) or FMRF-NH₂ (SEQ ID NO:4), the viable cell count ranges from

IN THE CLAIMS

1. (Amended) A gene coding for a pentapeptide having an amino acid sequence of Asp-Ile-Leu-Arg-Gly (SEQ ID NO:1) and a molecular weight of 570.959, wherein the C-terminal is amidated.

2. (Amended) The gene as set forth in claim 1, wherein the pentapeptide has dormancy-control activity

3. (Amended) The gene as set forth in claim 1 or 2, wherein the pentapeptide is derived from pre-larvae of *Antheraea yamamai*.